

Figure 1



09858289 . 032003

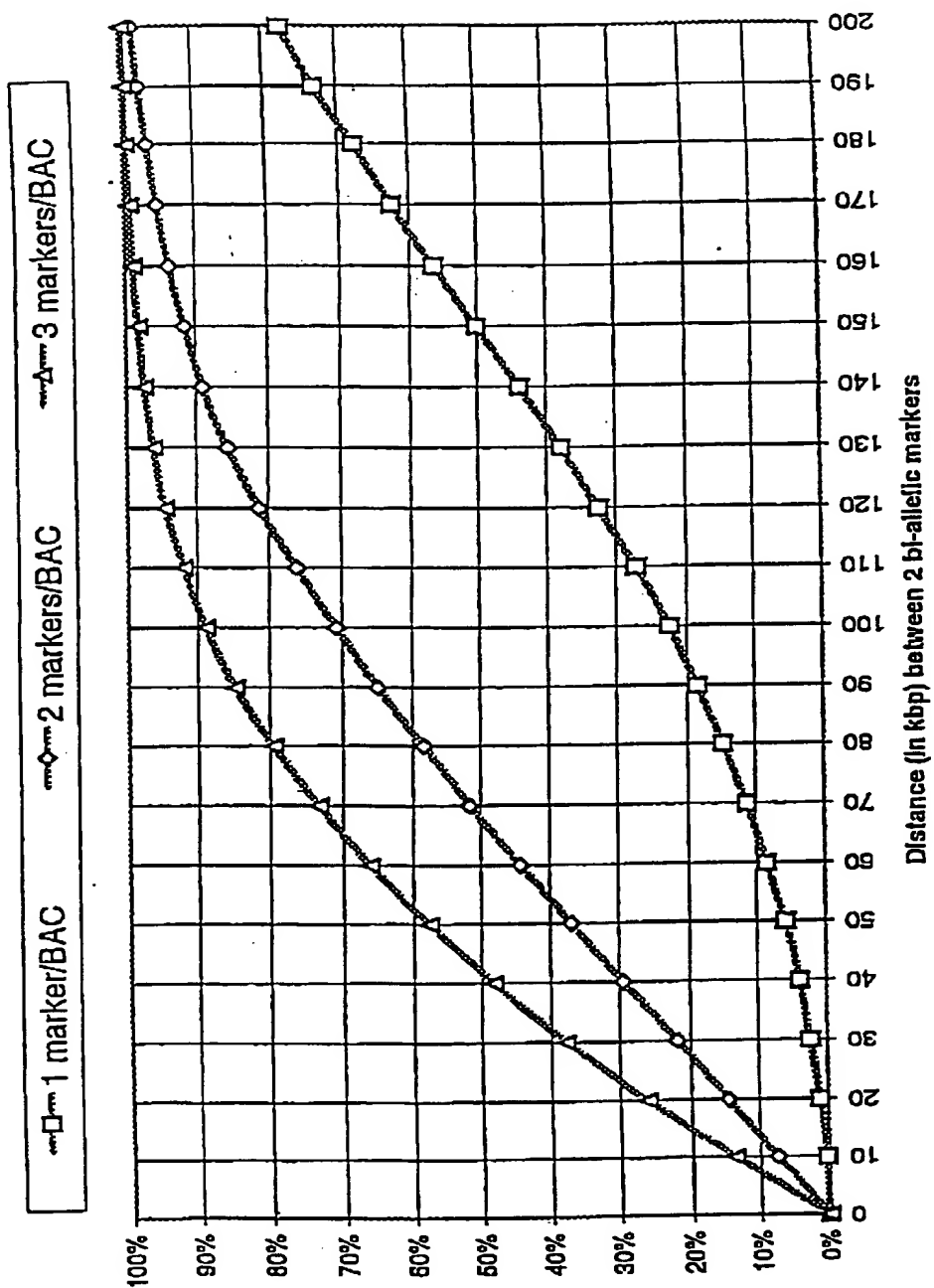


Figure 2A



09858289.032003

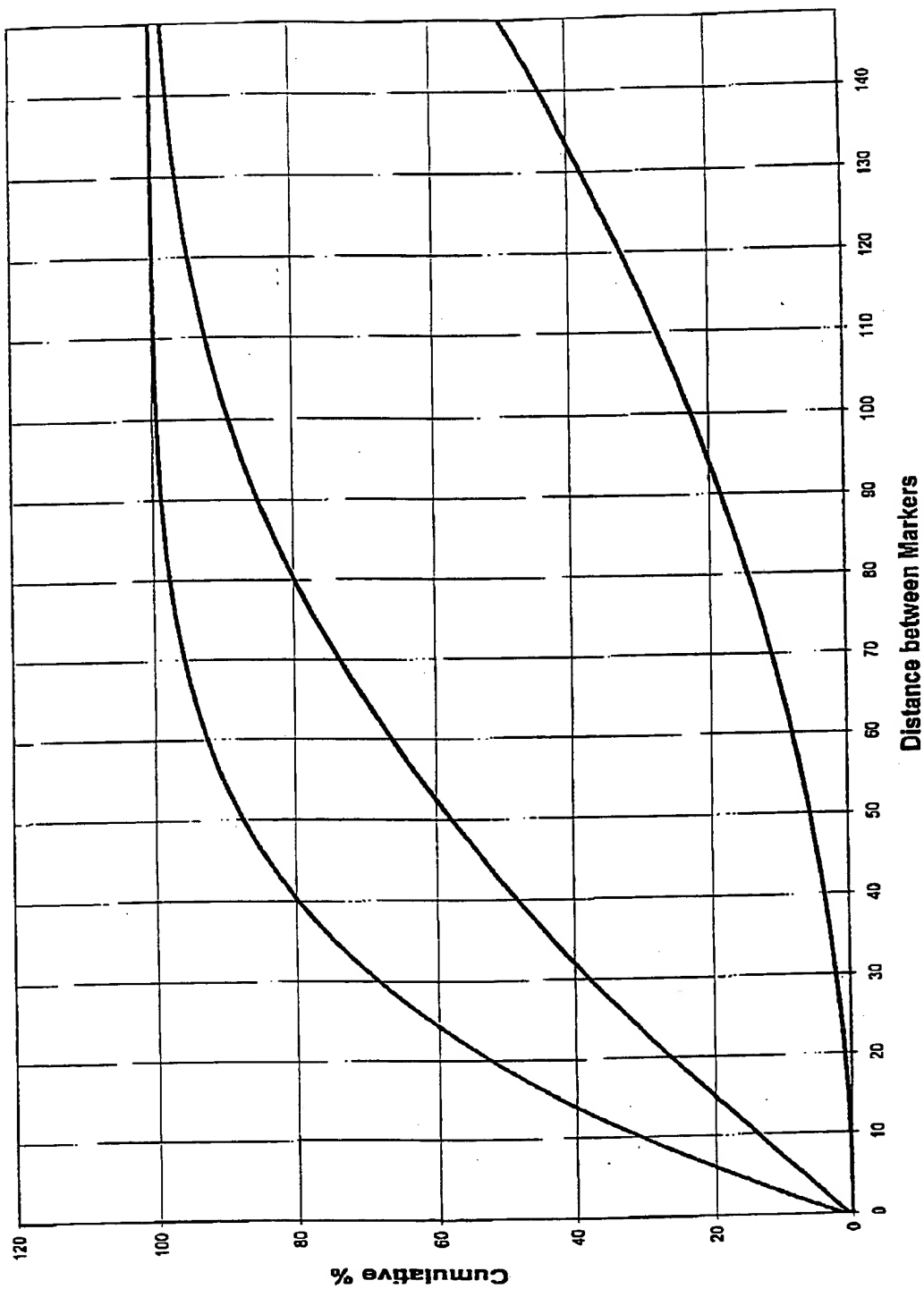


Figure 2B

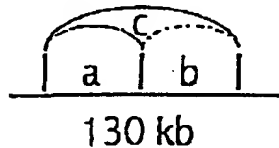
— 1 marker/BAC
— 3 markers/BAC
— 6 markers/BAC



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LD in a random French caucasian population

- 54 sized « random » BACs covering 8100 kb
- 213 SNP ; 2 to 6 / BAC, mean allele frequency = 0.3
- Order and distance unknown
- For 1 BAC :



* \overline{m} intermarker distance : $130/3 = 43$ kb

* \overline{m} LD strength estimate : $m(a,b,c) = 0.51$

- For 54 BACs :

* \overline{m} intermarker distance = 38 kb

* \overline{m} LD strength estimate = 0.63 ± 0.05
(324 pairs)

- For 19 unlinked SNPs : m LD strength estimate = 0.12 ± 0.007
(171 pairs)

Figure 2c



059587009 - 0320003

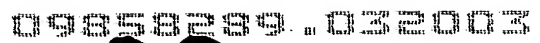
p-VALUE DISTRIBUTION

# aff	150										
# non aff	150										
	pAi	non aff	0	0,1	0,2	0,3	0,4	0,5			
Δ pAi		0,05	8,77E-05	0,06407752	0,14252002	0,19106311	0,21543442	0,22009395			
Δ pAi		0,1	1,91E-08	0,00080384	0,00467774	0,01023571	0,01382303	0,01382303			
Δ pAi		0,15	3,06E-12	1,3319E-06	3,8827E-05	0,0001478	0,0002343	0,00020218			
Δ pAi		0,2	3,22E-16	9,1413E-10	9,0305E-08	5,733E-07	9,6336E-07	5,733E-07			
Δ pAi		0,25	2,08E-20	2,2614E-13	6,2679E-11	5,873E-10	8,7113E-10	2,5396E-10			
Δ pAi		0,3	7,82E-25	2,152E-17	1,3261E-14	1,5189E-13	1,5189E-13	1,3261E-14			
Δ pAi		0,35	1,62E-29	7,9823E-22	8,4152E-19	9,1669E-18	4,2713E-18	5,5844E-20			
Δ pAi		0,4	1,73E-34	1,1282E-26	1,524E-23	1,1488E-22	1,524E-23	1,1282E-26			

# aff	200										
# non aff	200										
	pAi	non aff	0	0,1	0,2	0,3	0,4	0,5			
Δ pAi		0,05	5,92E-06	0,03250945	0,09039173	0,13111935	0,15260313	0,15678006			
Δ pAi		0,1	8,65E-11	7,4765E-05	0,00109084	0,00302886	0,00447365	0,00447365			
Δ pAi		0,15	8,02E-16	2,3653E-08	2,0257E-06	1,1771E-05	2,1573E-05	1,7772E-05			
Δ pAi		0,2	4,18E-21	1,5375E-12	6,7374E-10	7,764E-09	1,5417E-08	7,764E-09			
Δ pAi		0,25	1,13E-26	2,525E-17	4,4025E-14	8,5532E-13	1,4423E-12	2,8148E-13			
Δ pAi		0,3	1,47E-32	1,1488E-22	5,8424E-19	1,4886E-17	1,4886E-17	5,8424E-19			
Δ pAi		0,35	8,62E-39	1,4784E-28	1,5457E-24	3,6958E-23	1,3394E-23	4,197E-28			
Δ pAi		0,4	2,09E-45	5,2308E-35	7,6438E-31	1,1224E-29	7,6438E-31	5,2308E-35			

aff affected Individuals
non aff non affected Individuals
pAi non aff allele frequency in non affected Individuals
Δ pAi % Difference in allele frequency between affected and non-affected individuals

Figure 3 (I)



# aff	500
# non aff	500
	pAI non aff
Δ pAI	0,05
Δ pAI	0,1
Δ pAI	0,15
Δ pAI	0,2
Δ pAI	0,25
Δ pAI	0,3
Δ pAI	0,35
Δ pAI	0,4

	0	0,1	0,2	0,3	0,4	0,5
	8E-13	0,00072323	0,00741965	0,0169842	0,02371865	0,02516449
	1,07E-24	3,7948E-10	2,4176E-07	2,7579E-06	6,9679E-06	6,9679E-06
	3,81E-37	1,0719E-18	5,8344E-14	4,2622E-12	1,8601E-11	1,1611E-11
	2,99E-50	5,0895E-29	1,6881E-22	6,9321E-20	3,7441E-19	6,9321E-20
	4,27E-64	7,2043E-41	7,7528E-33	1,194E-29	4,3462E-29	7,6438E-31
	9,7E-79	3,9328E-54	6,3017E-45	1,9429E-41	1,9429E-41	6,3017E-45
	2,91E-94	6,8513E-69	8,7878E-59	2,3478E-55	1,8839E-56	1,1206E-62
	9,5E-111	7,7199E-85	1,8063E-74	1,4484E-71	1,8063E-74	7,7199E-85

# aff	affected individuals
# non aff	non affected individuals
pAi non aff	allele frequency in non affected individuals
Δ pAi	% Difference in allele frequency between affected and non-affected individuals

Figure 3 (II)



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ALLELIC ASSOCIATION
3,000 MARKERS MAP

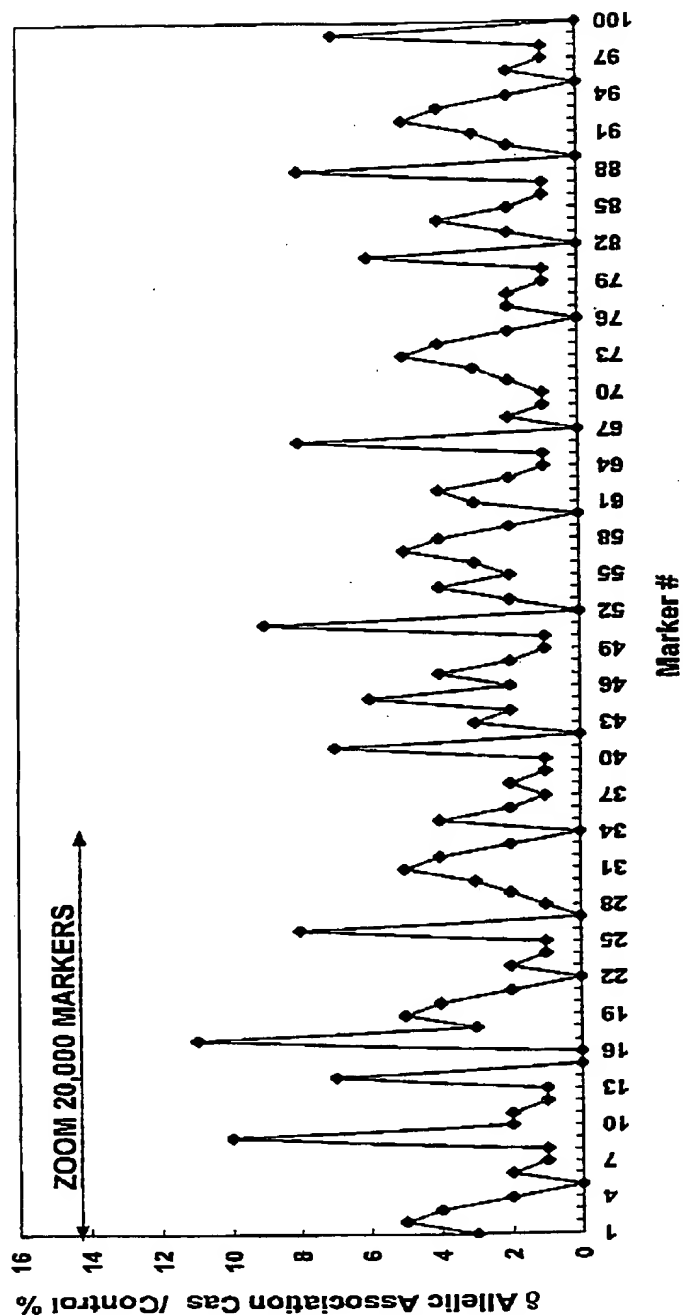


Figure 4



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ALLELIC ASSOCIATION 20,000 MARKERS MAP

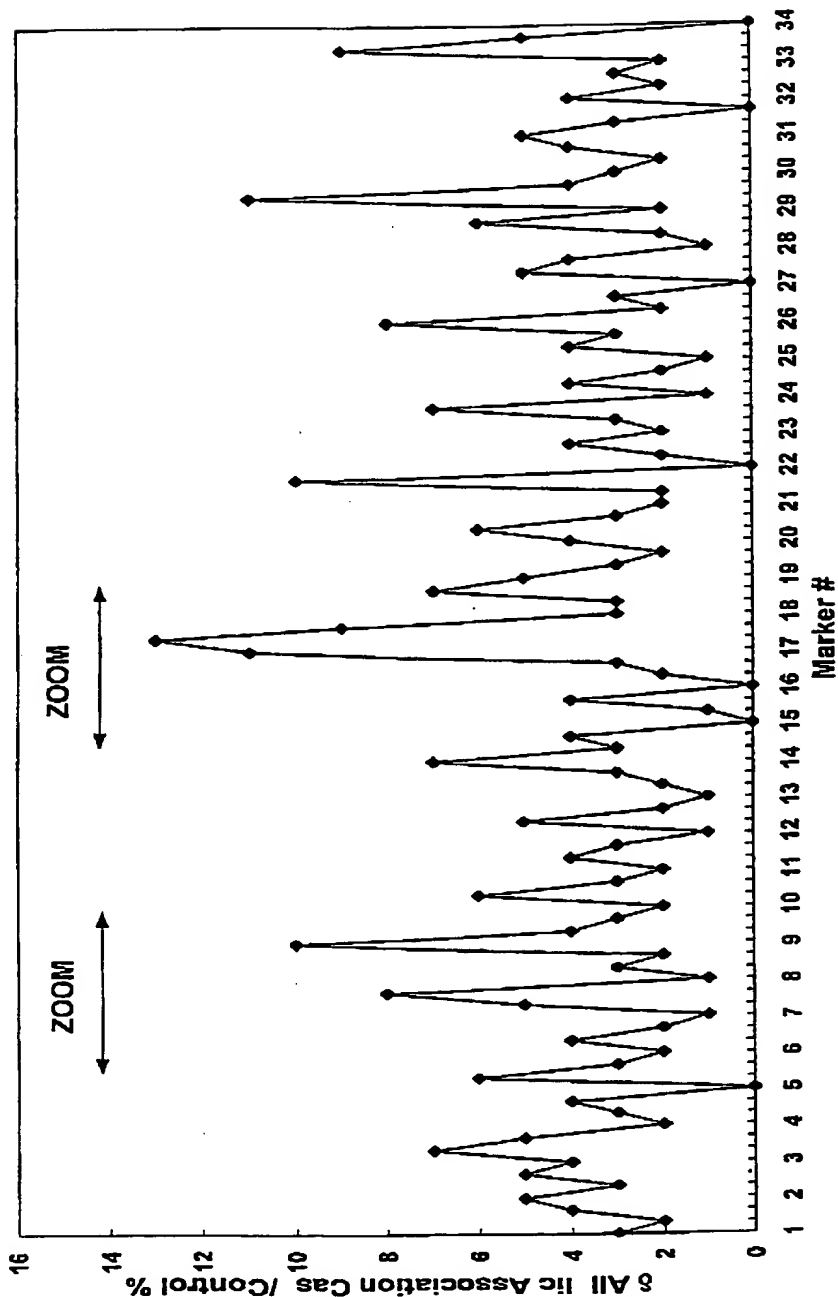


Figure 5



ALLELIC ASSOCIATION 60,000 MARKERS MAP

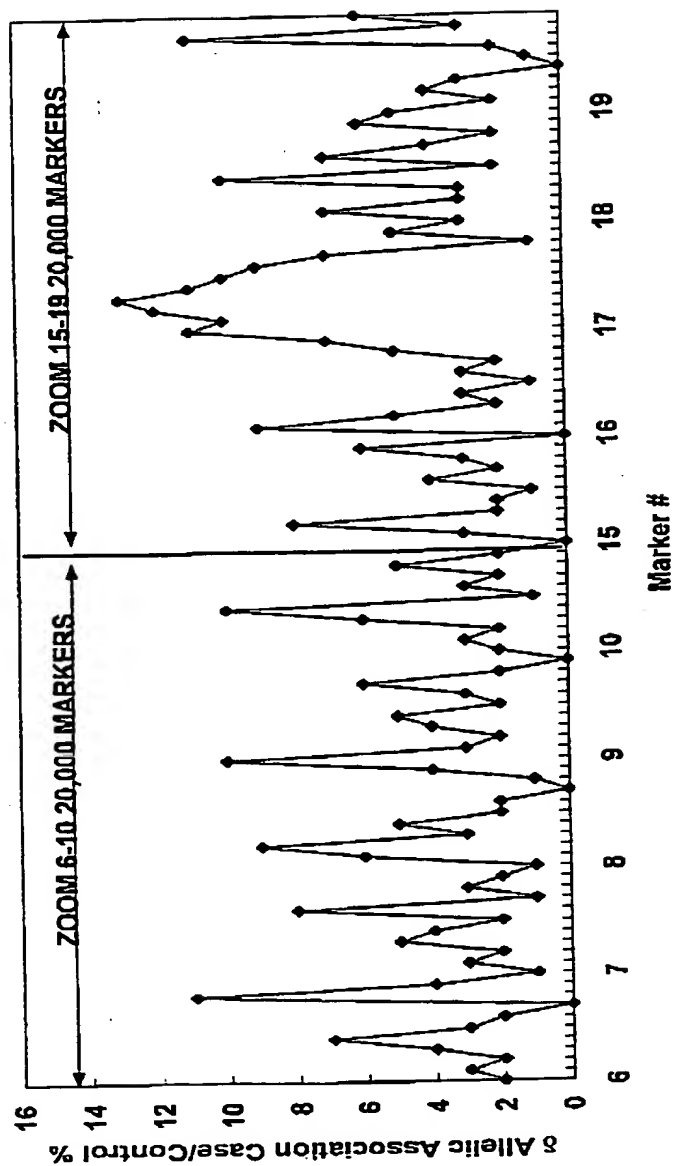


Figure 6



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APO E REGION HAPLOTYPE FREQUENCY ANALYSIS

POPULATIONS		AD CASES (225)				AD CONTROLS (248)			
markers	99-366	99-344	99-359	99-355	haplotype frequencies	odds-	P value		
p value	3,01E-01	1,11E-01	6,63E-01	1,38E-01	cases	ratio			
haplotype 1	C	G			0,404	1,52	3,05E-03 ***		
haplotype 2		G	A		0,203	1,29	1,24E-01 *		
haplotype 3			G	G	0,375	1,36	2,83E-02 **		
haplotype 4	C		A		0,264	1,36	5,95E-02 **		
haplotype 5		G		A	0,116	1,70	1,64E-02 **		
haplotype 6	C			A	0,15	1,19	3,59E-01 *		
haplotype 7	T		G	G	0,225	2,09	4,76E-05 *****		
haplotype 8	T	A	G	G	0,228	2,44	2,05E-06 *****		

Figure 7



APO E REGION HAPLOTYPE SIMULATION POPULATION : 225 CASES vs 248 CONTROLS

Haplotype	4 Markers				haplotype frequencies		odds-ratio	pvalue
	A	T	G	G	cases	controls		
99-344/439	99-366/274	99-359/308	99-355/219		0,228	0,108	2,44	2,05E-06 *****

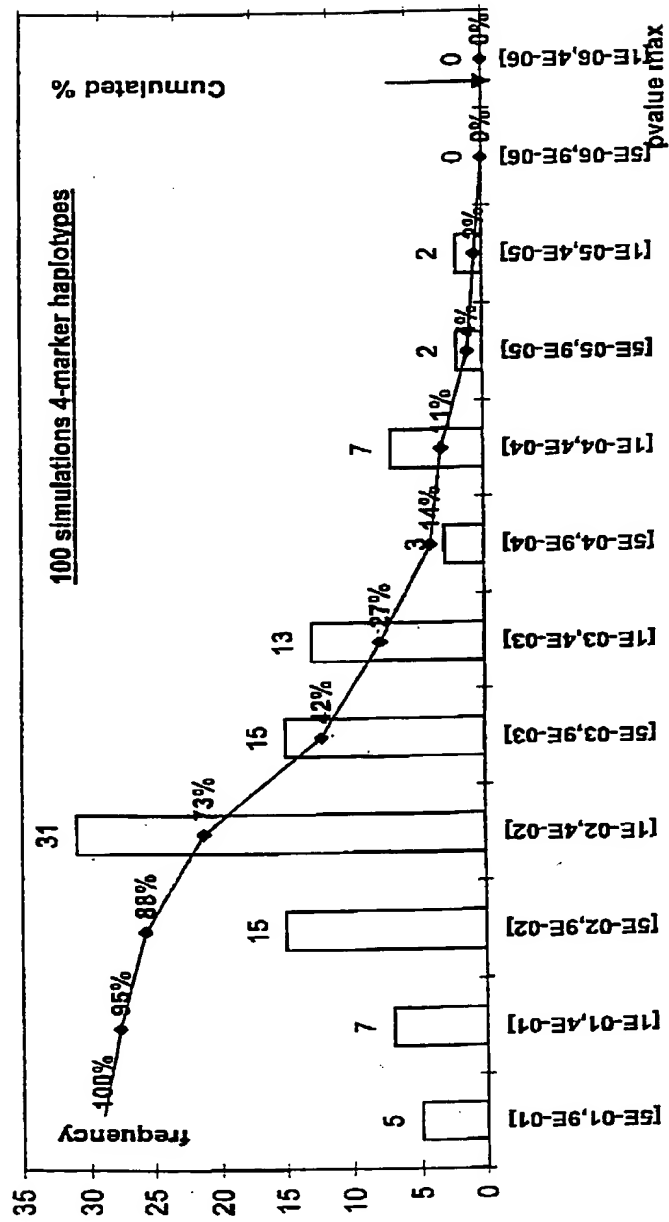


Figure 8

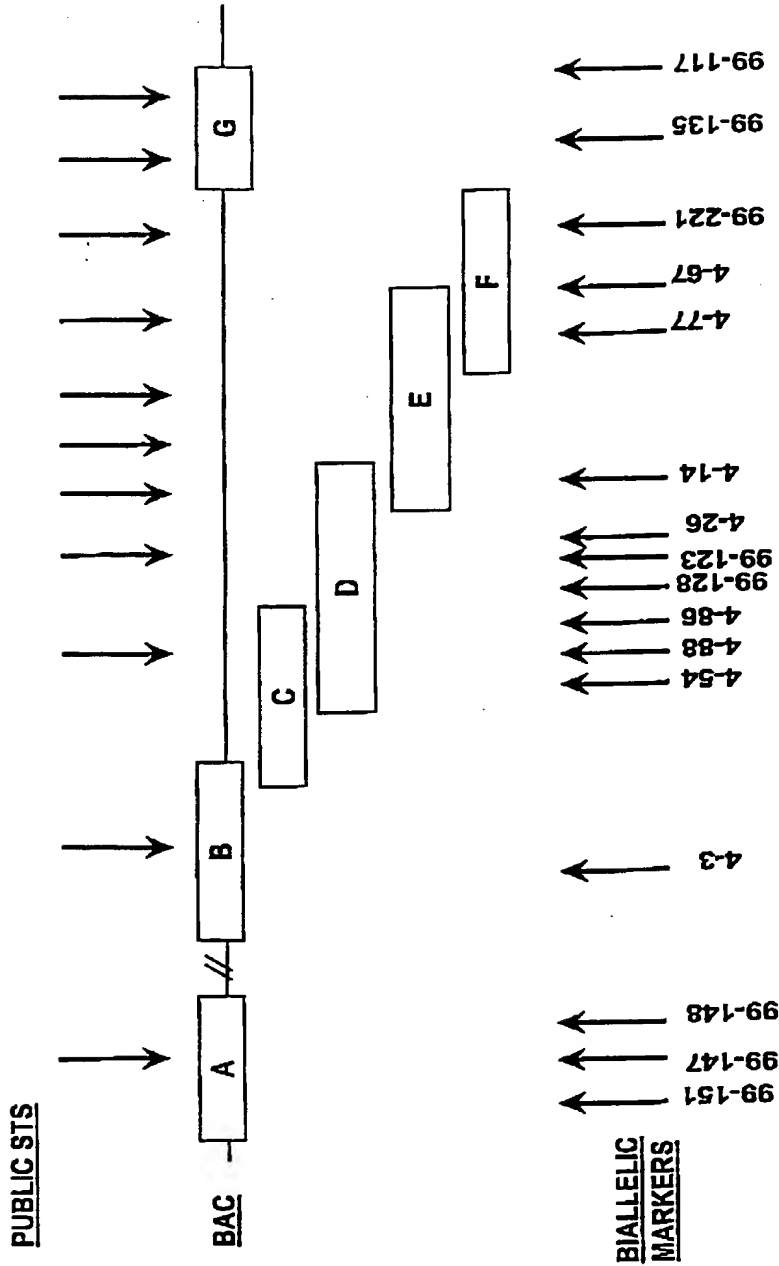


Figure 9



09858289 - 09800X

PROSTATE CANCER ASSOCIATION STUDIES (FIRST SCREENING)

Population	PROSTATE CANCER	NON AFFECTED
Sample size	CASES = 112	CONTROLS=76
Population	35 sporadic cases	> 65 years
Characteristics	+ 77 familial cases	PSA<4

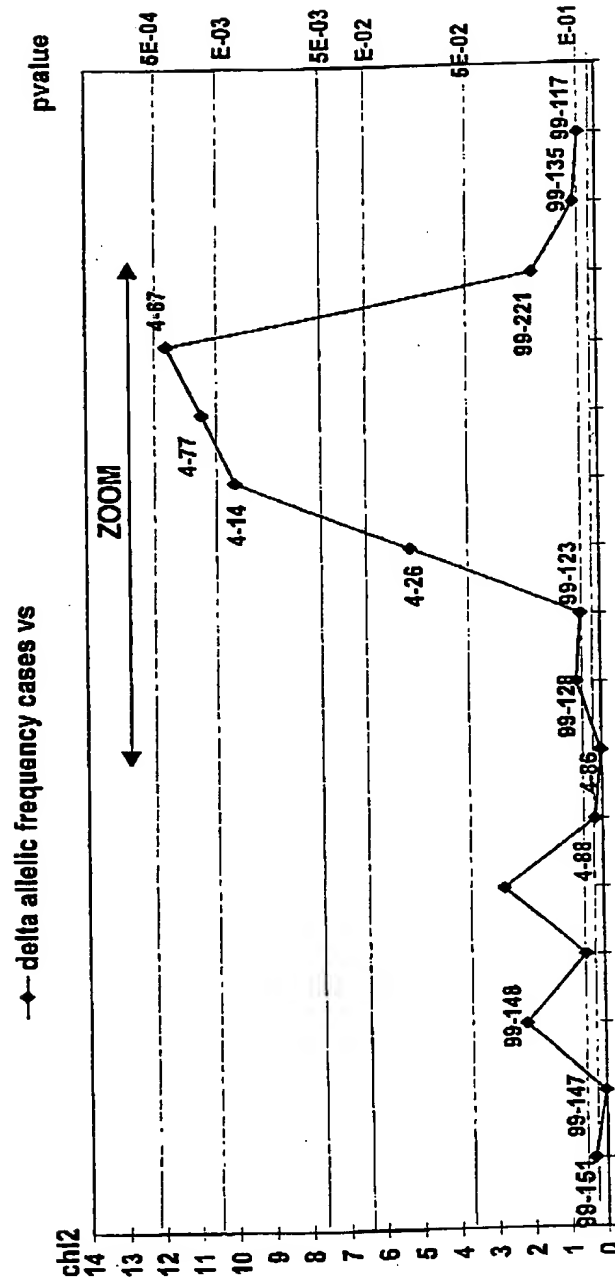


Figure 10



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PROSTATE CANCER ASSOCIATION STUDIES (ZOOM)

	PROSTATE CANCER	NON-AFFECTED
	CASES (185)	CONTROLS (104)
characteristics of populations	47 sporadic cases + 138 familial cases	> 65 years PSA<4

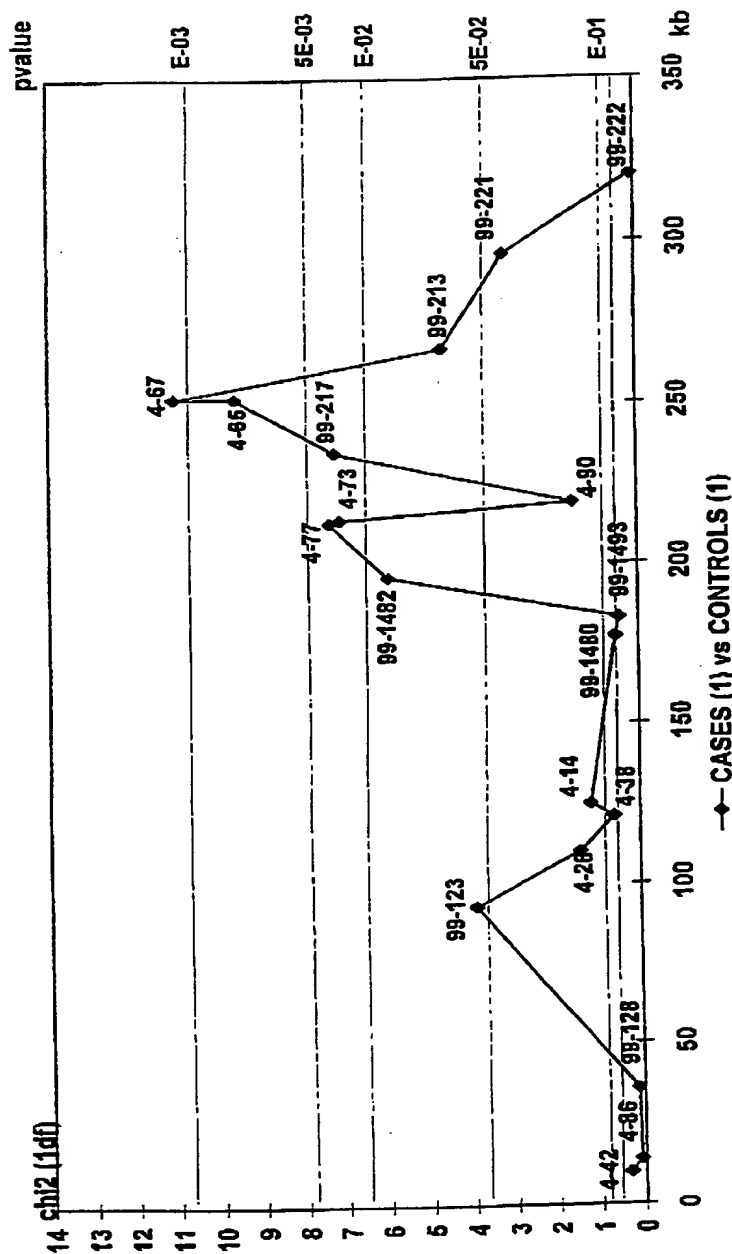


Figure 11



PROSTATE CANCER HAPLOTYPE FREQUENCY ANALYSIS

	PROSTATE CANCER		NON-AFFECTED	
	CASES (281)		CONTROLS (130)	
characteristics of populations	143 sporadic cases + 138 familial cases		> 65 years PSA<4	

markers	99-123	4-26	4-14	4-77	99-217	4-67	99-213	99-221	99-135	haplotype frequencies	relative risk	pvalue
	H0287B09	B0189E08	B0463F01									
genes	←-----PG1-----→											
p value	2,00E-01	1,00E-01	1,00E-01	2,00E-02	2,00E-02	6,00E-04	9,00E-02	7,00E-01	2,00E-01	cases	controls	
haplotype 8 >304kb<	C	A	C	G	T	T	C	A	A	0,075	0,018	9,00E-04 ***
haplotype 7 >286kb<		A	C	G	T	T	C	A	A	0,085	0,016	6,00E-05 ****
haplotype 6 <186kb>		A	C	G	T	T	C	A	A	0,116	0,019	1,00E-05 ****
haplotype 5 <171kb>			C	G	T	T	C	A	A	0,117	0,013	9,00E-07 ****
haplotype 4 <83kb>				G	T	T	C	A	A	0,117	0,025	2,00E-05 ****
haplotype 3.1 <54kb>					T	T	C	A	A	0,117	0,027	2,00E-05 ****
haplotype 3.2 <54kb>				G	T	T	C			0,222	0,109	4,00E-05 ****
haplotype 2.2 <39kb>				G	T	T				0,251	0,134	2,00E-04 ****
haplotype 2 <32kb>					T	T	C			0,226	0,112	1,00E-04 ***
haplotype 1.1 <17 kb>					T	T				0,256	0,148	3,00E-04 ****
haplotype 1.2 <15 kb>					T	T	C			0,233	0,129	6,00E-04 ***

Figure 12

09050200 - 030000



PROSTATE CANCER HAPLOTYPE SIMULATIONS (100 ITERATIONS)

markers	4-14	4-77	99-217	4-67	99-213	99-221	haplotype frequencies		relative risk	pvalue
							cases	controls		
haplotype	C	G	T	T	G	A	0,117	0,013	10,06	9,00E-07

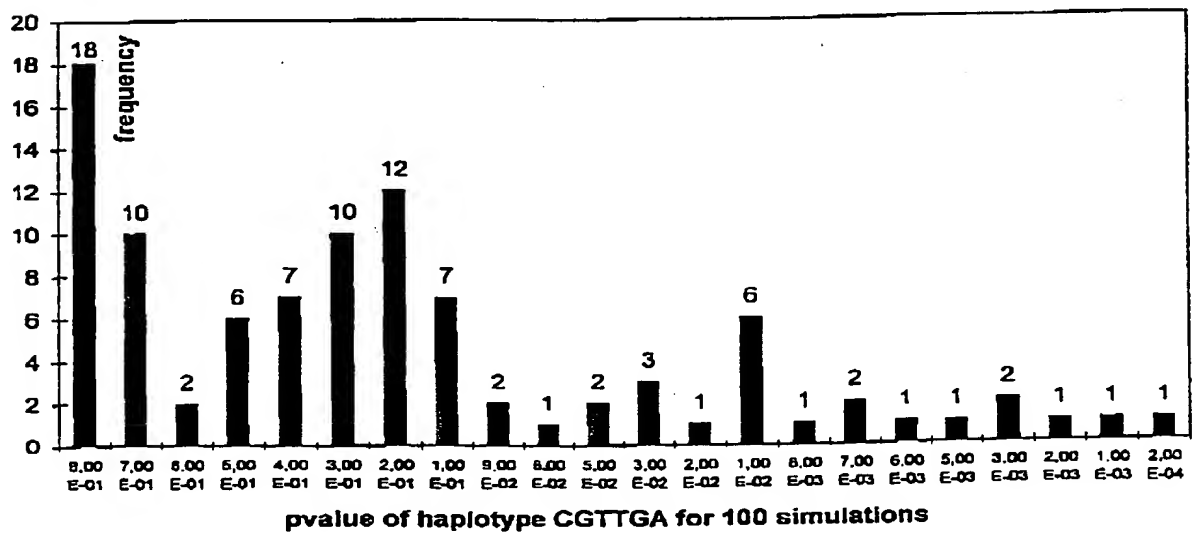
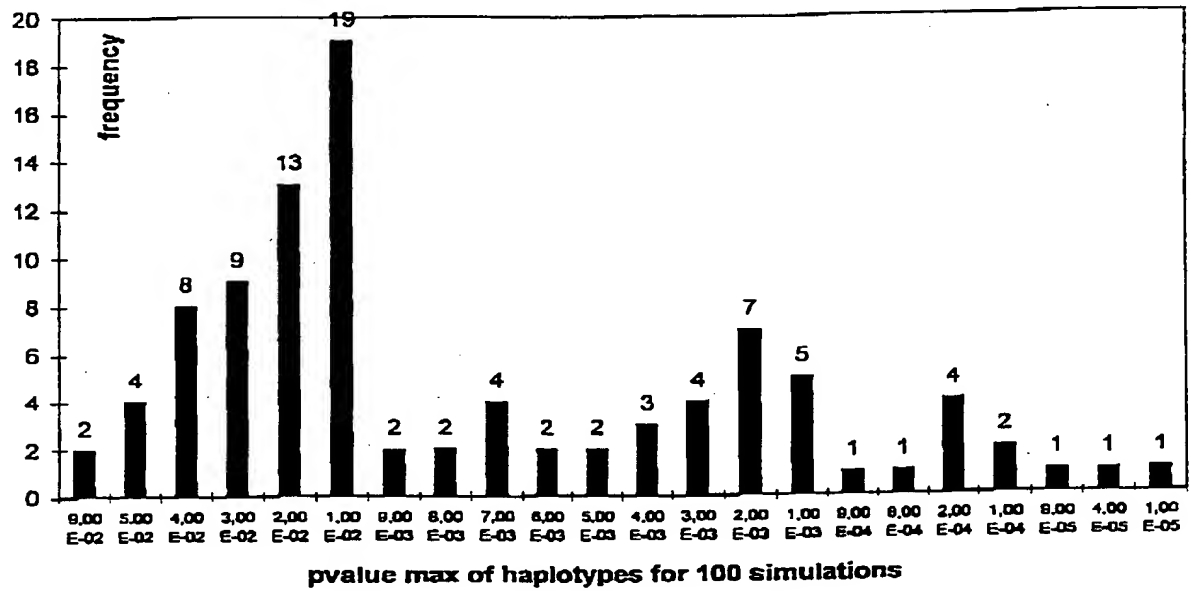


Figure 13



AVERAGE LD PATTERN GENOMIC HETEROGENEITY

Recombination rate	Lower A	Higher B
Nb markers	89	69
All SNP	0.61 (749)	0.42 (1190)
Rare < 0.2 Rare vs rare	0.75 (65)	0.17 (158)
Frequent > 0.2 Frequent vs frequent	0.51 (410)	0.49 (544)
Rare vs frequent	0.72 (274)	0.41 (488)

FIGURE 14

**Exonic/nonexonic LD**

	Nb pairs	Average intermarker distance	Average LD
Exonic SNPs	36	26 kb	0.65 ± 0.021
Non exonic SNPs	60	36 kb	0.48 ± 0.018
Exonic/Non exonic	96	32 kb	0.60 ± 0.015

FIGURE 15

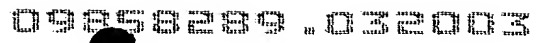


FIGURE 16 A



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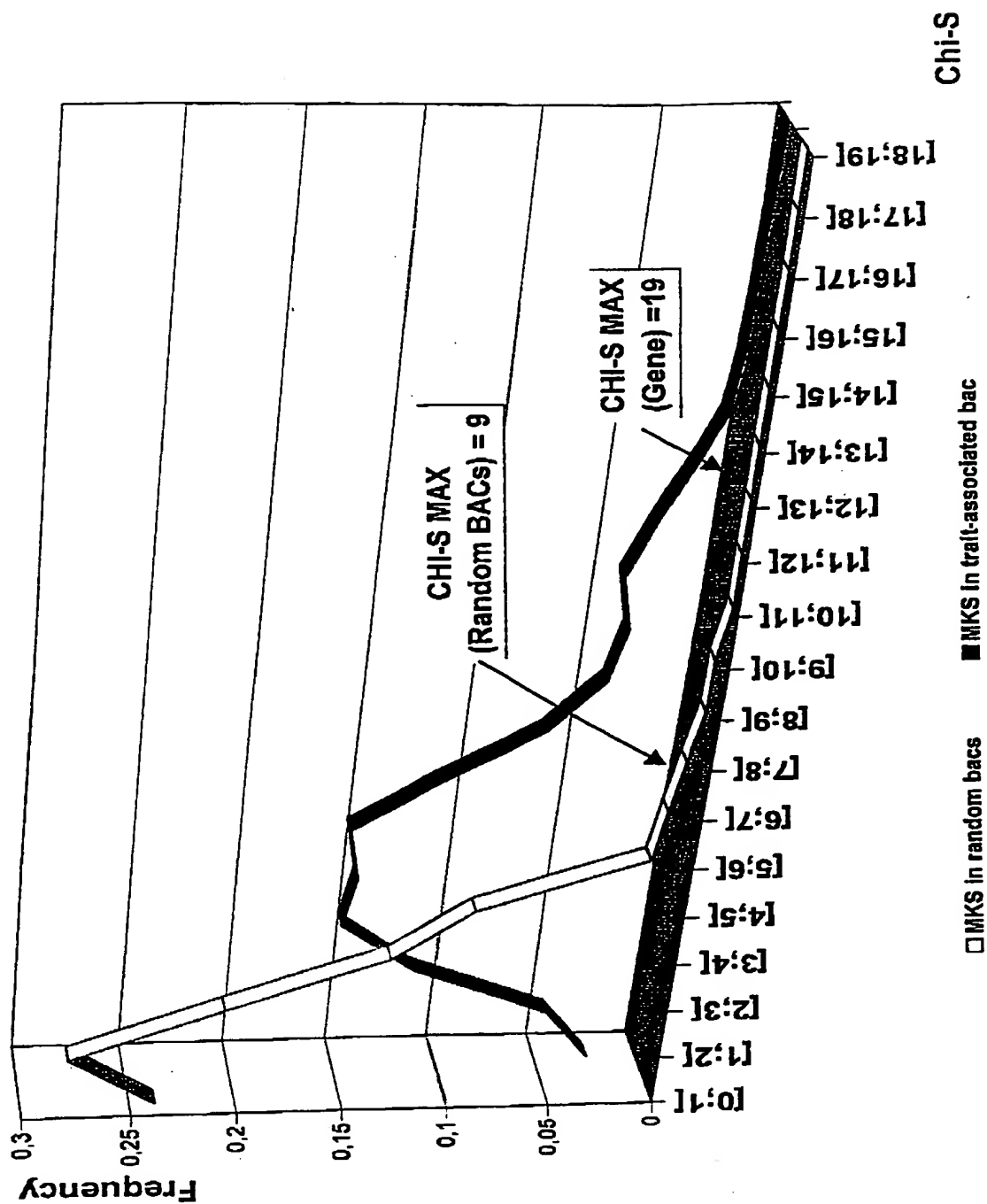


FIGURE 16B



09859299.032003

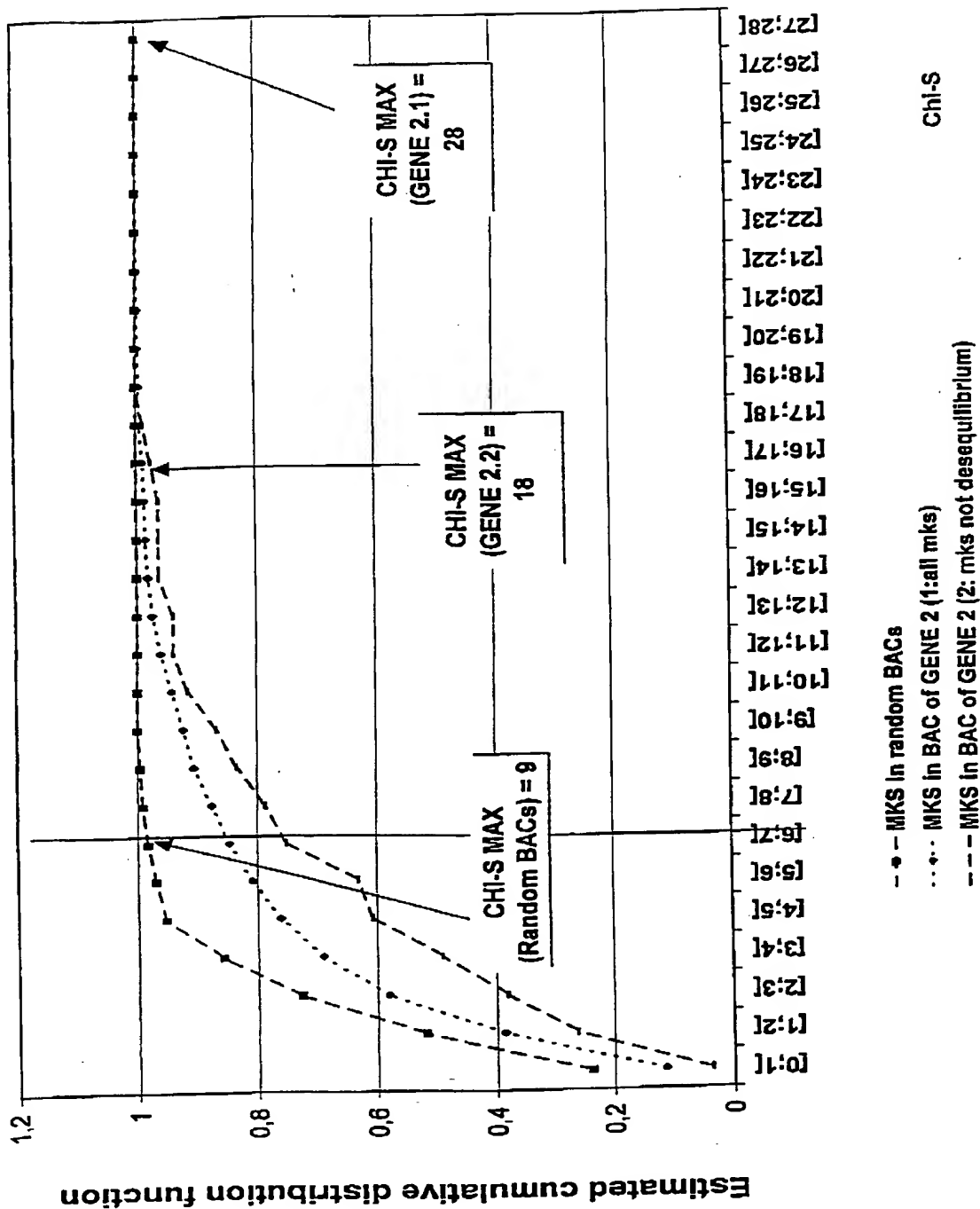


FIGURE 17A



09858289 032003

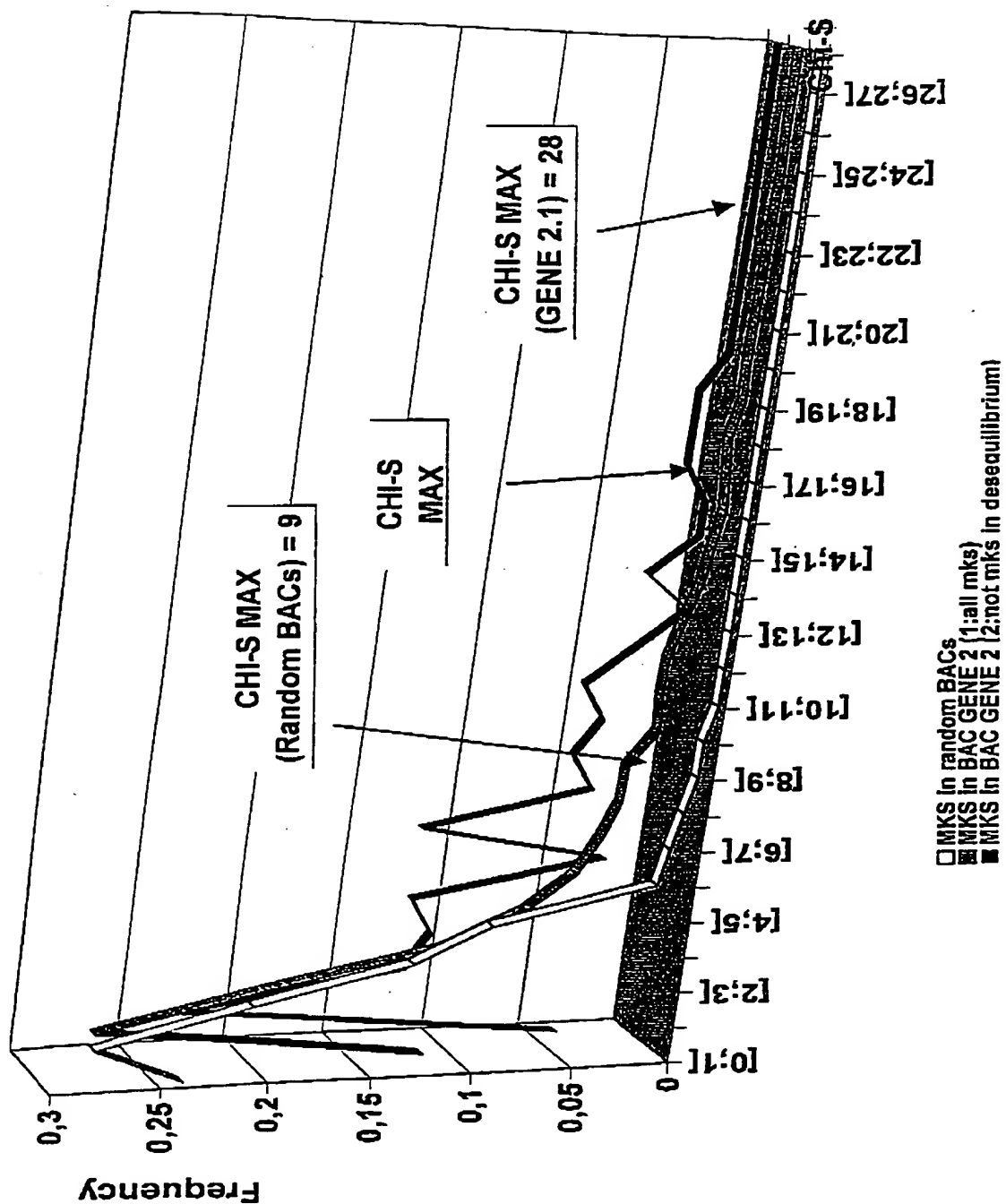


FIGURE 17 B

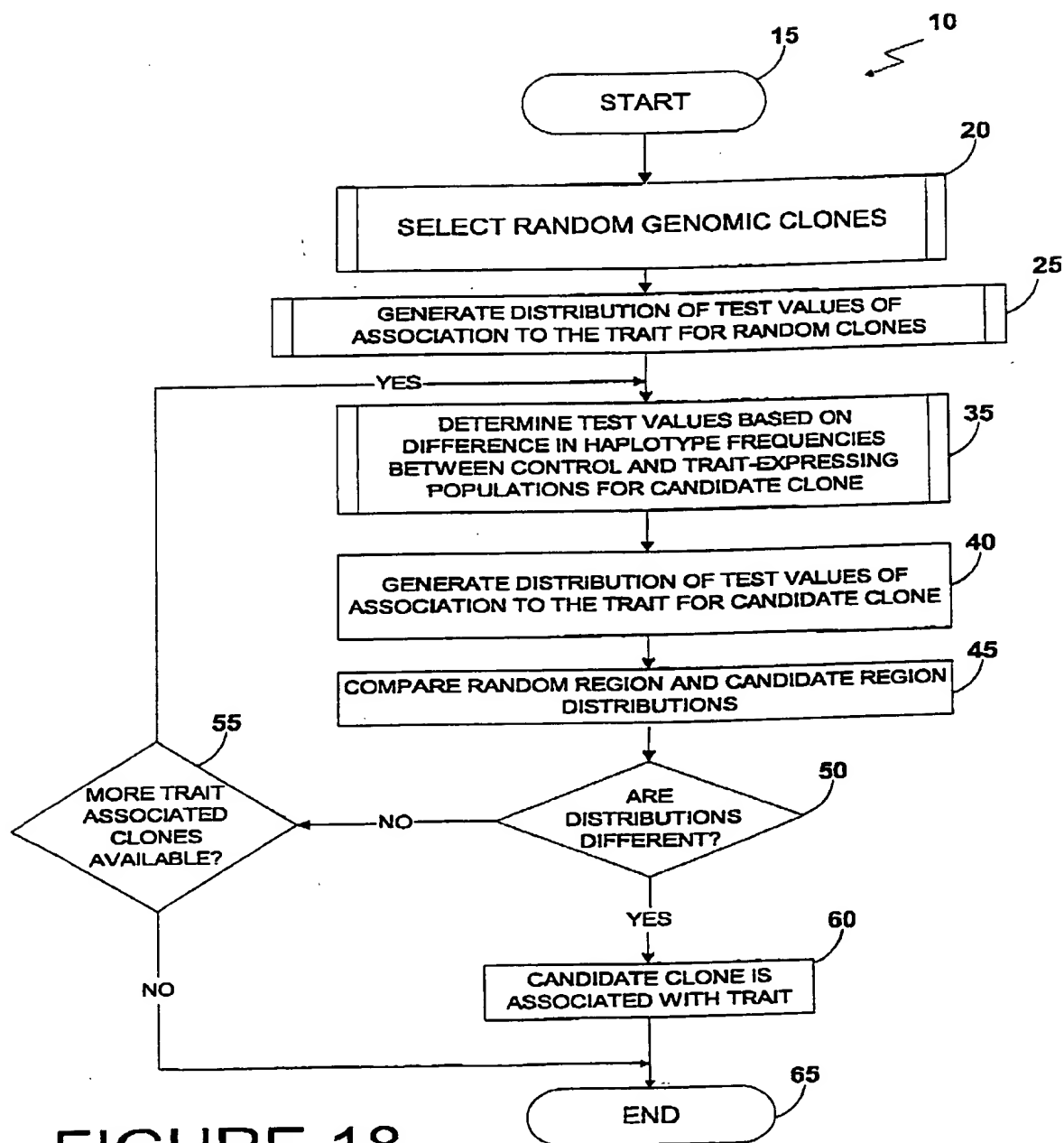


FIGURE 18

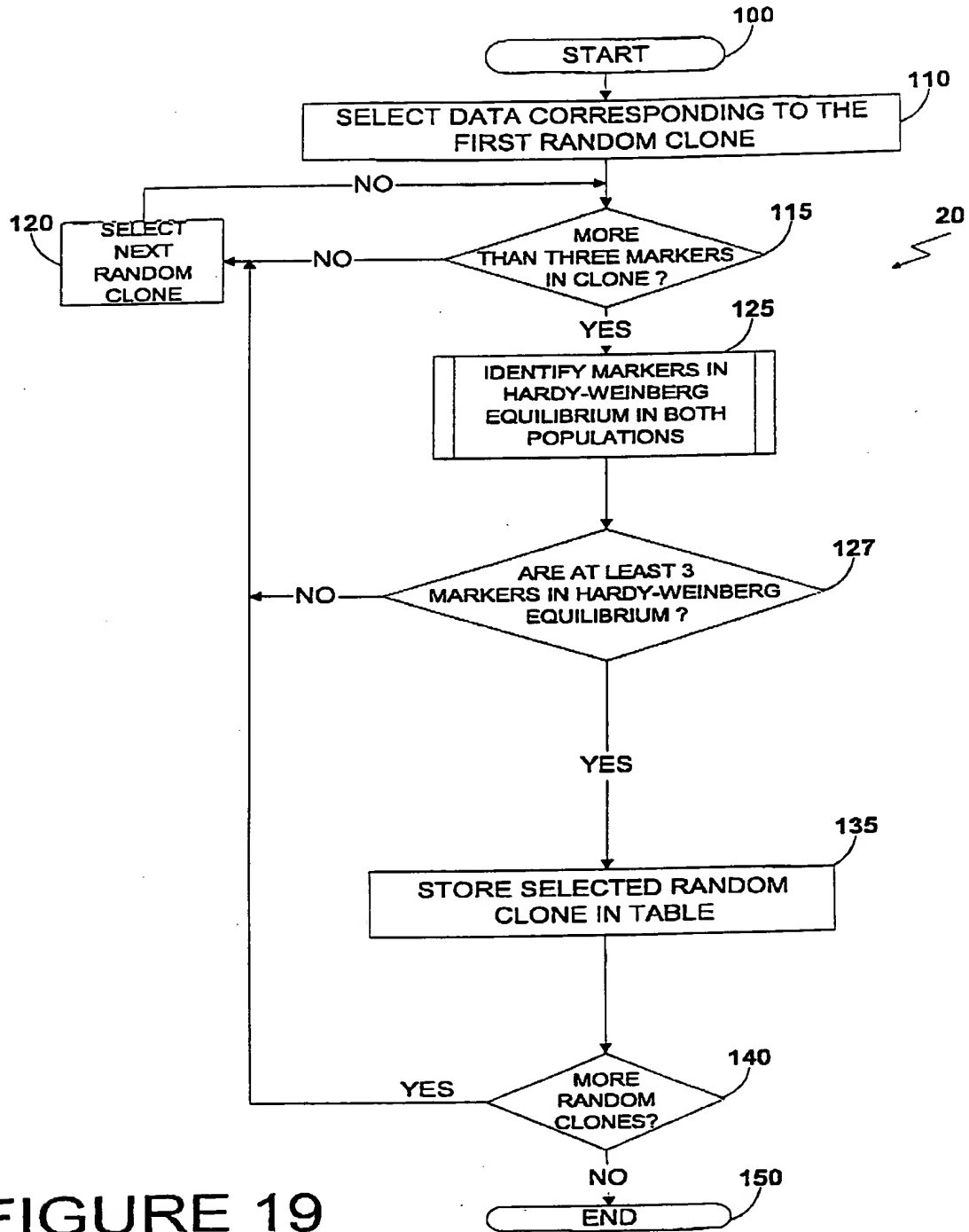


FIGURE 19

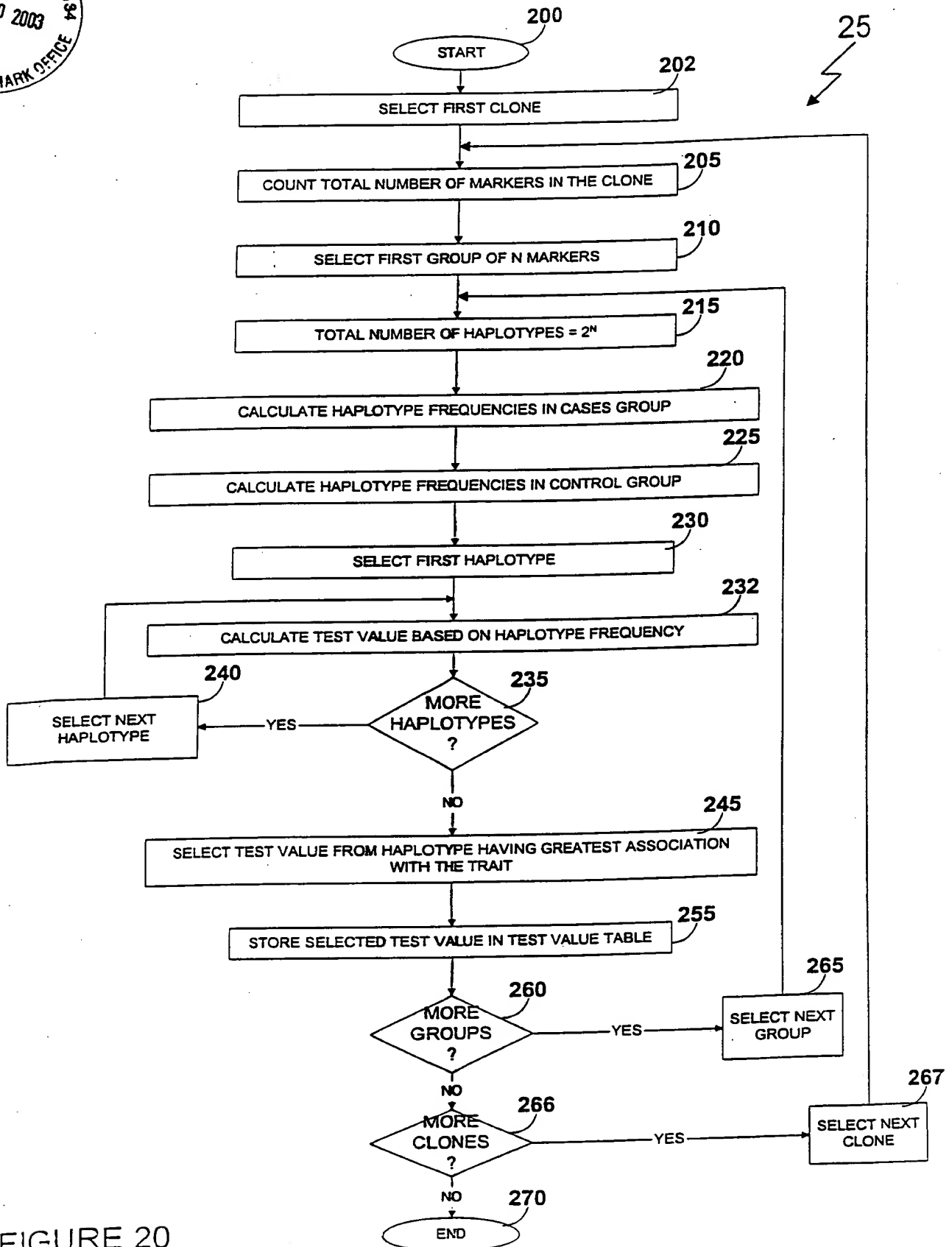
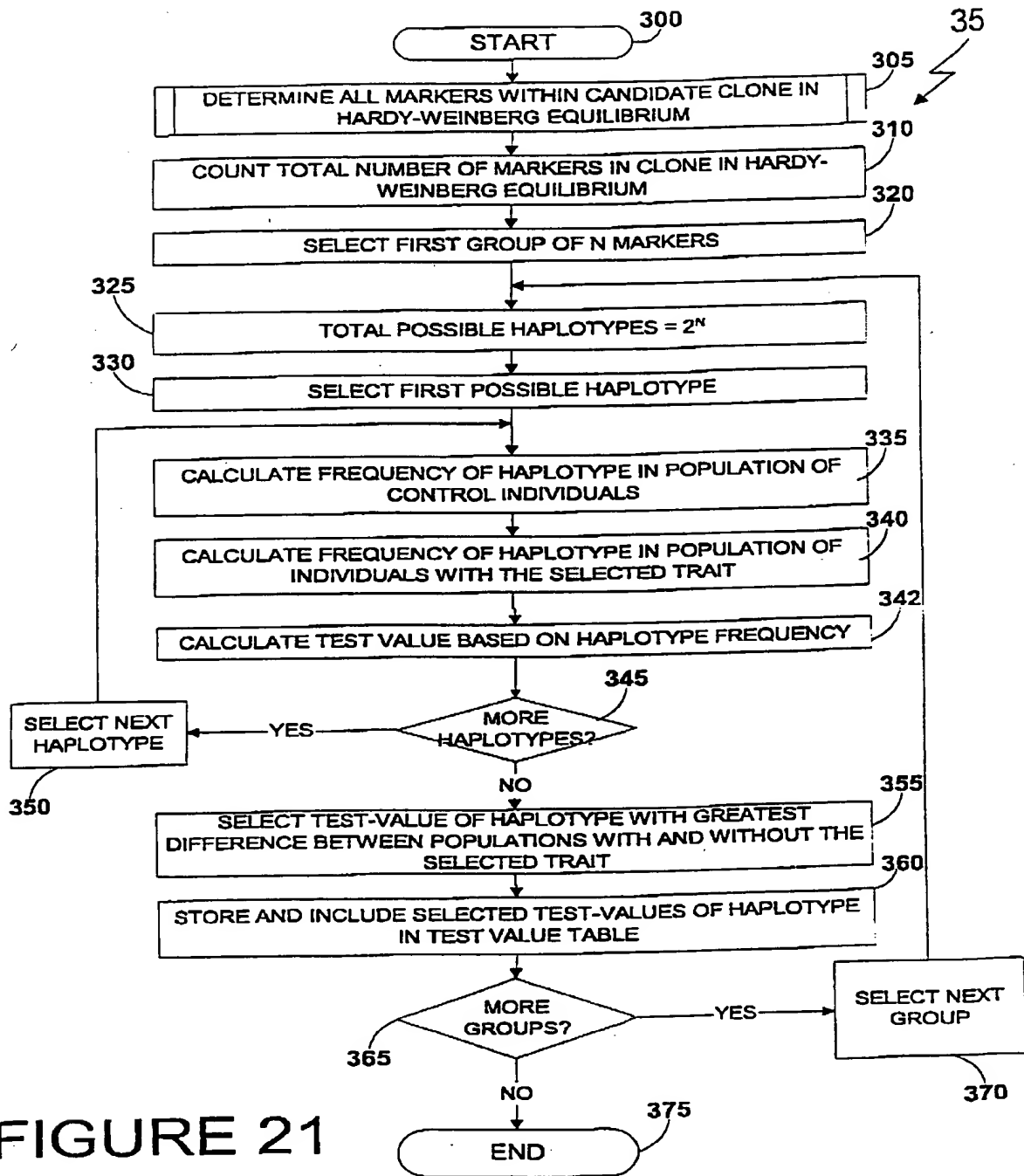


FIGURE 20



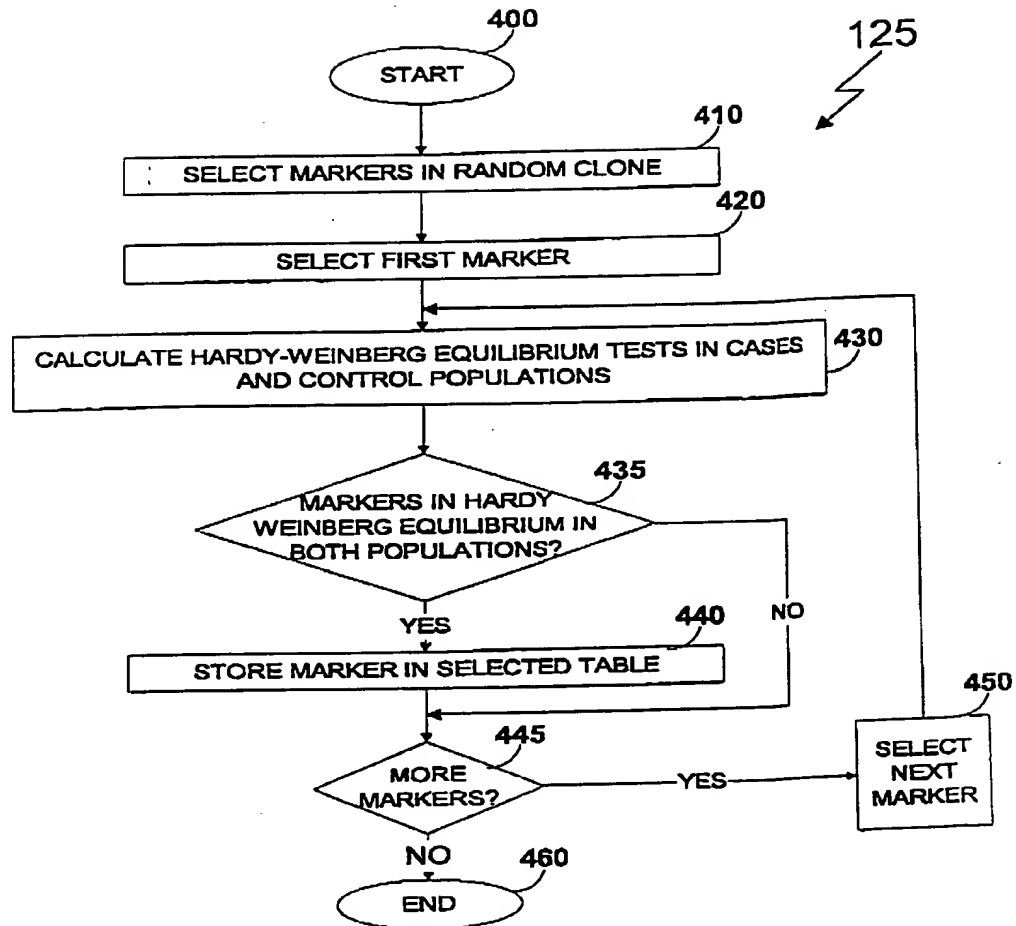


FIGURE 22

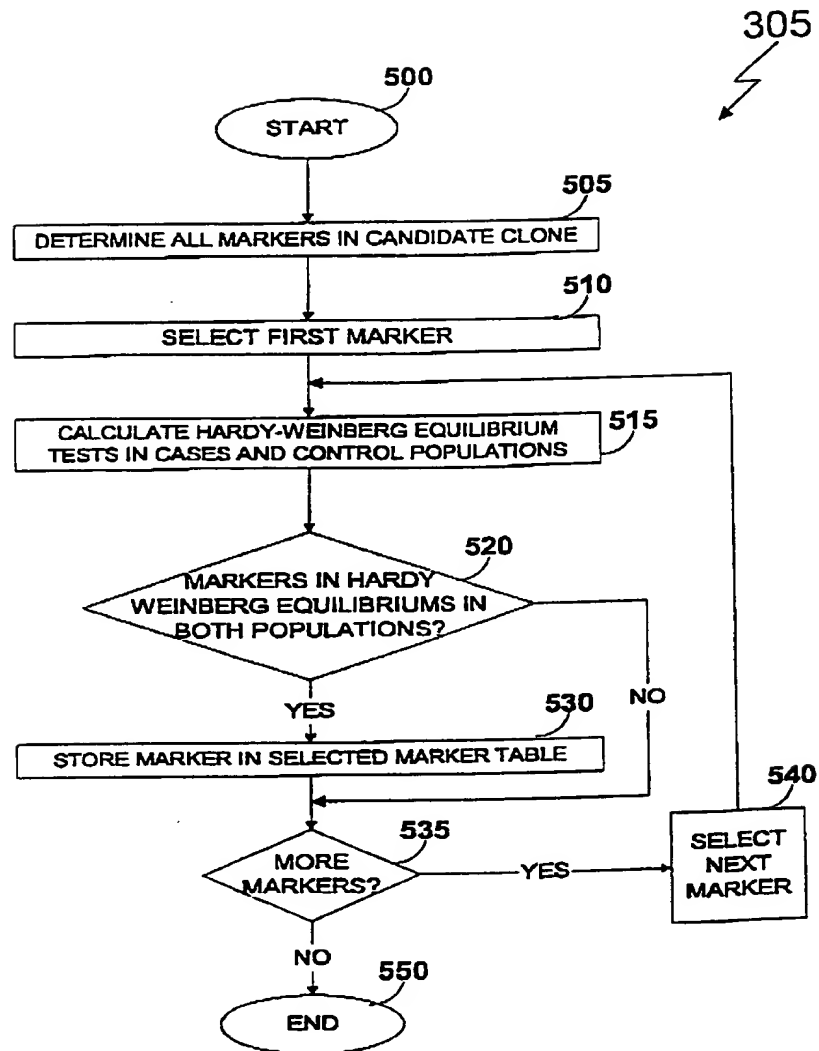


FIGURE 23

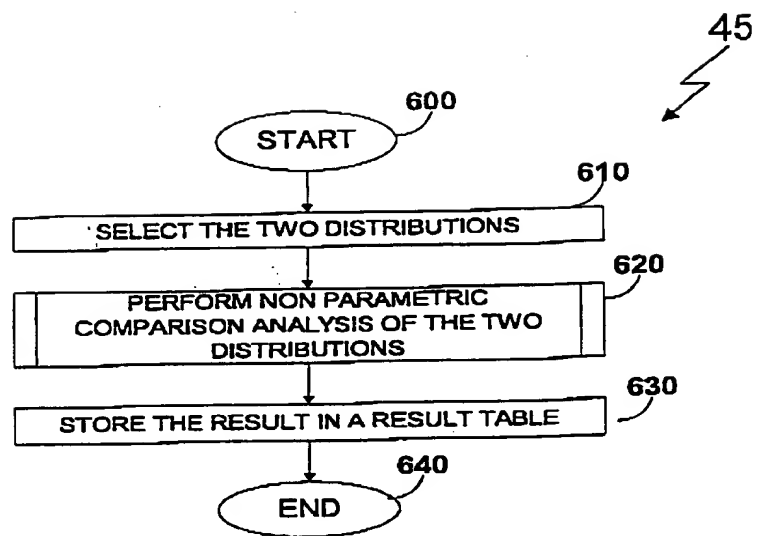


FIGURE 24

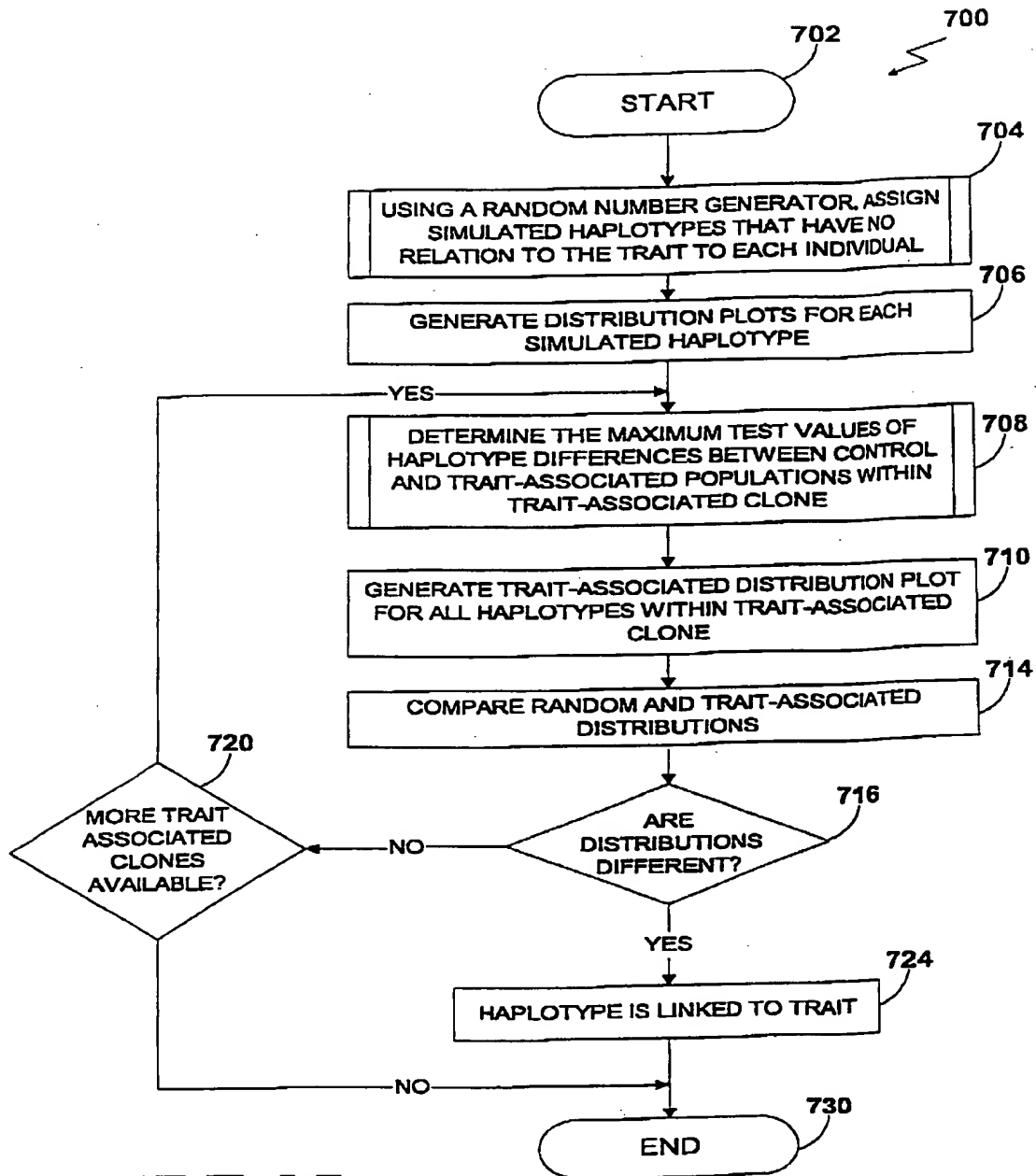


FIGURE 25